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14. ABSTRACT The goal of the 01-05 TATRC grant to the University of Oregon (UO) was to support the mission of the UO's Brain Biology and Machine Initiative (BBMI) of establishing a world-leading center linking genomic and proteomics to human cognitive neuroscience research. Toward this overall goal, the TATRC grant provided the following key support: 1. The establishment of a 3 Tesla Brain Imaging Center for scanning of human and animals. 2. The installation of high speed computing infrastructure for the integration of fMRI and EEG signals to provide informatics support to the initiative. 3. The development of a center for genomic and proteomic research by making links between individual researchers and the centralized genomic facility. 4. The development of a mammalian genetics center. 5. Support of research projects that move toward the vertical integration across many levels of analysis to link work in genomics and proteomics to studies of cognitive neuroscience. 6. Support recruitment and hiring new faculty to enhance the mission of the BBMI.		
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## **Introduction**

The goal of the 01-05 TATRC grant to the University of Oregon (UO) was to support the mission of the UO's Brain Biology and Machine Initiative (BBMI) of establishing a world-leading center linking genomic and proteomics to human cognitive neuroscience research. Toward this overall goal, the TATRC grant provided the following key support:

1. The establishment of a 3 Tesla Brain Imaging Center for scanning of human and animals.
2. The installation of high speed computing infrastructure for the integration of fMRI and EEG signals to provide informatics support to the initiative.
3. The development of a center for genomic and proteomic research by making links between individual researchers and the centralized genomic facility.
4. The development of a mammalian genetics center.
5. Support of research projects that move toward the vertical integration across many levels of analysis to link work in genomics and proteomics to studies of cognitive neuroscience.
6. Support recruitment and hiring new faculty to enhance the mission of the BBMI.

## **Body**

### **Academic Year 01-02**

The University of Oregon (UO) was awarded \$2.7 million from the DoD (Telemedicine and Advanced Technology Research Center- TATRC) to establish a neuroimaging center housing functional magnetic resonance imaging (fMRI) instrumentation capable of measuring dynamic processes in the human brain with high temporal and spatial resolution. The fMRI center began operations at the UO in the Spring of 2002, with additional support provided through competitive federal grants, as well as private contributions totaling \$6.5 million through 2004. The neuroimaging and cognitive neuroscience research programs examined fundamental processes that give rise to human thought and behavior. Examples include integration of motor and sensory control, memory retrieval and forgetting, the neurobiology of emotions, and the development of language. DoD funding of an additional \$0.5 million supported the expansion of the fMRI projects and the formal establishment of the Lewis Center for Neuroimaging (LCNI) in 2002. Experimental techniques were developed for manipulating sensory, perceptive and cognitive processes so that they can be imaged selectively in the fMRI.

### Proposed Major Task

- a. Construction and Installation of fMRI unit with implementation of necessary technological accessories such as eyetracking components, servers, subject monitoring systems, etc.

### Accomplishments

The fMRI was operational by March 2002. The ancillary equipment was available in late June 2002. Ancillary equipment included the successful integration and implementation of the stimulus response systems, eye-tracking system, subject physiologic monitoring system, the set up of the image analysis laboratory and the RF coil laboratory and the acquisition of initial structural and functional MRI data from human and non-human subjects.

Funding from nonTATRC sources to support the fMRI center included a \$10 million gift from a private donor, the Lewis family, which included direct support for infrastructure and quasi-endowment support for operational activities.

Interdisciplinary research training in the form of three workshops for the faculty and research staff at the UO was conducted: a) the basics of fMRI; design and construction of RF coils; and the use of specific software tools for the analysis of fMRI data.

Work began on the implementation of electrophysiological data acquisition done simultaneously with the fMRI. Circuit designs for filtering the MRI-induced signals in the electrophysiological leads were shared with Professor Nikos Logothetis of the Max Planck Institute (Germany) for testing in human and primate studies.

Began work on the development of the automated and semi-automated edge-detection software. Concurrently, the staff developed a fully functional program for converting the industry standard DICOM image files into other commonly used image files for data analysis programs.

### **Academic Year 02-03**

The major objectives supported by the \$1.8 million in support from TATRC in FY2002 were the core research activities in the Lewis Neuroimaging Center (LCNI) and Neuroinformatics Centers (NIC), and the expansion of the scope of existing programs through additional faculty

recruitment and technical support. Additionally, technology transfer opportunities were developed, such as specialized instrumentation to enhance fMRI imaging capabilities, and computational methods for telemedicine applications such as the evaluation of victims of acute stroke or head trauma. Further collaborative interactions with the TATRC research group in aspects such as medical imaging and informatics were explored during this period. In collaboration with the LCNI, the NIC submitted a \$1.5 million proposal to the NSF in January 2003 to acquire a high performance computational network to address neuroimage analysis. At the time, faculty directing the NIC had approximately \$1.2M in competitive grants related to this work.

### Proposed Major Tasks

funding to support work in Cognitive Neuroscience

funding to support infrastructure and research projects at the newly developed Neuroinformatics Center

funding to support new faculty recruitment and start-up

### Accomplishments

a. In this academic year Neuroscientists from a number of areas worked on projects essential to the complex story of how neural networks develop in areas ranging from auditory perception to cognitive control. The reports in this section illuminate the efforts of the BBMI researchers to explore the physical basis of networks underlying significant normal functions and their disorders. These reports mainly focus on the study of mechanisms of selection and volition, orientation, and genetics.

*Helen Neville* and her associates examined how precise auditory localization develops in human infants (Wood, et al, 2002) and they studied the role visual input has in the development of auditory localization by comparing the process in sighted people with those born blind. These studies have shown evidence of adaptation of visual areas to processing of peripheral auditory signals (Neville & Bevalier, 2002).

The visual system must figure out what objects are present with often very complex scenes. *Margaret Sereno* and colleagues (Sereno, et al 2002) used computerized displays to give the impression of depth. They carried out fMRI analysis with monkeys to reveal the precise but distributed brain areas involved in representing stimuli in three dimensions. They have provided needed anatomical links between human and animals and have shown the importance of 3 D representation, not only for awareness of what stimulus is present in the scene, but also to organize action toward the stimulus.

One the earliest and most important actions that human infants make is to point. Intentional pointing in infants is found during the latter half of the first year and becomes a critical feature in interaction between caregiver and infant often called joint attention. *Lee and Van Donkelaar* (2002) report that it is possible to create temporary disruptions of the network that controls pointing by stimulation over both dorsal and ventral occipital area in the general areas where *Sereno* showed 3D vision is computed. In a behavioral study, *Dassonville & Bala* (2003) find that both ventral and dorsal visual systems are normally involved in responses to common visual input. They explore the effects of a visual illusion and show that both reaching and identification are influenced in the same way by the illusion. These studies suggest important commonalities

between the networks for perception and action that will have to be reflected as we work to understand how genes and experience influence these early developing functions.

For many years psychologists have sought the mechanisms by which one can control the access of memory to consciousness. *Michael Anderson* (Anderson, et al, 2003) reported results showing that the instruction to avoid consciousness of a memory both reduces the success of later recall and activates a specific network of prefrontal cortex and hippocampus previously related to cognitive control of conflict between brain systems and learning. The studies suggest mechanisms by which trauma, hypnotic suggestion and other poorly understood environmental influences can alter brain networks.

Luu, et al, 2003 have shown that one of the areas involved in *Anderson's* study (anterior cingulate gyrus) is also important for the detection of error. By recording from multiple scalp electrodes, these authors show that adjacent areas of the ACC are involved in both cognitive emotional regulation that occur as a consequence of the error. Error detection can be studied easily in adults, infants and animals and thus provides a common method for examining brain areas involved in self-regulation.

It appears that some of these prefrontal regulatory areas are involved in a wide range of tasks that may be unique to human beings. These have been the target areas for a number of new paradigms and models that have been developed by BBMI researchers. For example *Ulrich Mayr* argues that some of these areas are important when learning requires integration of signal across modalities (Keele, et al, 2003) and Neville and associates report on the activity of these areas during language task (Woods, et al, 2002).

*Marrocco* reported that local infusion of scopolamine into the lateral intraparietal cortex of monkeys alters their ability to orient to visual signals. Marrocco previously found norepinephrine influences the ability to attain the alert state with a warning signal, but does not change orienting. They conclude that under their conditions, activity mediated by muscarinic cholinergic receptors within the intraparietal cortex is necessary for normal covert orienting while influencing norepinephrine transmission influences alerting. These findings are important both in showing the separate modulation of the two attentional networks and in efforts to examine the influence of cholinergic and noradrenergic genes on visual attention.

A paper by *Ed Awh*, (Awh et al, 2003) found that orienting to objects in space operates at least in part by suppression of the influence of distracters. In a related study using combined ERP/MEG methods Vogel (Hopf, et al, 2002) found sources within the ventral visual stream are involved in a task requires the discrimination of an object from others in the surround. These studies point the way to understanding attentional function in terms of biochemical pathways and provide important clues toward making the genetic analysis.

*Posner* and colleagues (Fan, et al, 2003) report that alleles of two genes, known to influence the efficiency of executive attention, also show differences in brain activation within the anterior cingulate when normal adults perform a task involving conflict. Both the MAOA and DRD4 gene influence dopamine transmission. The finding that they change activation in a brain area important for regulating many cognitive and emotional tasks provides an important link between genetic and brain imaging methods. Genes that relate to individual differences in attention are also likely to be important during the development of this network in early childhood.

Two recent projects take genetic behavior links even further. David Grandy, at Oregon Health Sciences University and now an adjunct professor in our new Mammalian Genetics Center, has created a mouse in which the DRD4 gene is deleted. This gene is important in executive attention and attention deficit disorder and its deletion results in signs of hyperactivity and learning deficits (Rubenstein, et al, 2001; Falzone, et al, 2002). Together with *Marrocco*, he proposed to examine how this deletion influences specific attentional networks in this knockout mouse model and *Kentros* planned to record electrical activity from cells in these mice.

*John Postlethwait* found that to a surprising degree the genetics of the zebrafish preserves aspects of chromosome organization found in the human (Fredriksson, et al, 2003). He is currently examining the stickleback fish as a possible entry into understanding the genetic basis of aggression. Genes controlling the construction, connectivity and activities of specific brain regions detect and interpret sign stimuli for aggression and mediate motor output. He expects to explore which genes are involved, the brain regions in which they act and what the genes do within these brain regions.

Genomic approaches are well-suited to assay the complex gene networks that underlie the complexity of the brain. *Chris Doe* has used DNA microarrays and bioinformatics to catalog the genes that make glia, a distinct cell type within the brain. His lab is currently working to dissect the genetic pathways that form various types of neurons using a type of DNA microarray produced only at the University of Oregon genomics facility. *Eric Johnson*'s lab has found that diverse physiological stresses—heat, heavy metal poisoning, low oxygen, caffeine, nicotine and carbon dioxide cause profound changes in gene activity, including a core group of genes that are activated by nearly all stresses.

*Rod Capaldi* reported on proteomic approaches to characterize the entire collection of proteins (the proteome) in human heart mitochondria (Taylor, et al, 2003a). Capaldi and colleagues have discovered that oxidative damage to the mitochondrial electron transport protein “Complex I” leads to neuronal cell death and the resulting neurodegeneration associated with diseases such as Parkinson’s and Alzheimer’s diseases (Taylor, et al, 2003b; Murray, et al, 2003a). It is anticipated that this methodology will lead to robust new clinical diagnostic tests as well as specific drug therapies for the corrections of these disorders.

The *van Donkelaar* lab has recently received two grants to examine aspects of functional recovery from either stroke or concussion. In the stroke project they use fMRI to examine how constraint-induced therapy induces changes in the patterns of activation during limb motion. The goal is to relate the degree of handedness prior to the stroke to the magnitude of the asymmetry in cortical activation before and after therapeutic intervention. This may have implications for the extent to which therapy is effective. In the concussion project they have demonstrated using the attention network task that the largest deficits are in the executive control of attention rather than in the orienting or alerting components. Measuring these effects over the course of a one-month recovery period should help in the understanding of the recovery process.

b. In 2002-2003, the NIC procured sun workstations and other networking equipment necessary to build up the infrastructure for the Neuroinformatics Center. Individuals were hired and supported to build the infrastructure, provide maintenance for the equipment and begin developing analytical tools related to the telemedicine projects and to work being done at the fMRI facility.

Further, the NeuroInformatics Center (NIC) worked on the design and development of a pilot telemedicine test bed that will link remote locations where EEG measurement experiments are conducted to a central facility where the EEG data will be analyzed. The test bed was to be built on a distributed computing platform and utilizes the internet for transferring of EEG and MRI data to the center and results to medical specialists. The project was worked on jointly between the NeuroInformatics Center and Electrical Geodesics, Inc. (EGI) which markets dense-array EEG systems.

Because of the extremely large data sets developed from fMRI and high density electrical recording, new computer technology was required to store the results and compute relationships between the activations developed by the two methods. The computer methods needed for carrying out these innovations involve massively parallel computation. Maloney & Shende (2003) explored the needed computer facilities and software. Together with colleagues at BBMI they received a 1.2 million dollar equipment grant from the National Science Foundation to implement these innovations within the BBMI program.

c. Funded the recruitment and start-up for two new faculty members, *Clifford Kentros* (Psychology) and *Victoria Herman* (Biology) whose research is relevant to the BBMI. In particular, Kentros was recruited by BBMI to serve as a principal investigator within the new mammalian genetics research center. In his postdoctoral work in the laboratory of Dr. Eric Kandel, Kentros investigated the relationship between neural plasticity and the formation and maintenance of a hippocampal representation of an environment with long-term unit recordings from behaving rodents. He found that the stability of a hippocampal representation of an environment requires selective attention to the available spatial cues and depends upon dopaminergic neurotransmission. These findings suggest important links between attention and memory and provide a powerful animal model for the exploration of the physiological and genetic basis for both of these highly interactive cognitive processes. Trained in molecular biology as well as electrophysiology, Kentros helped to begin set up of a core facility for the generation of transgenic mice via pronuclear injection.

### **Academic Year 03-04**

The DoD appropriations bill for FY03 included \$3 million for the BBMI to strengthen the connections between genetics and neuroscience research, both areas in which the UO has internationally recognized excellence. Pioneering research began to link genetic factors with complex traits such as personality, learning and attention. Connecting a broader range of disciplines under the BBMI allows UO researchers to probe genetic mechanisms underlying our uniqueness, both as individuals and as a species. Specific tasks addressed included: Enhance the basic infrastructure to identify specific DNA segments and to isolate associated proteins influencing behavioral traits and related brain functions or disorders (genomics and proteomics); and Exploit the ability to selectively manipulate and transplant individual genes in experimental animals to study how genetic factors affect brain function (transgenic).

### Proposed Major Tasks

funding to support work in genetics and proteomics including infrastructure support support for the fMRI facility and the use of the fMRI by BBMI affiliated faculty

Support for Transgenic Mouse Facility activities  
Project support for cognitive neuroscientists and relevant facilities  
Project support for NIC  
Education and Dissemination of information

### Accomplishments

a. The 03-04 grant provided partial support of the purchase of an FTICR mass spectrometer and HPLC interface. It also provided partial support for a technologist to set up and run the equipment and some support to pay for analysis costs borne by the faculty using the equipment.

Much of the development of the brain and aspects of behavioral control are regulated by gene expression. The genomics facility developed by *Eric Johnson* developed DNA microarrays for measuring gene expression on a global scale in eight model organisms in the past two years. These tools have furthered BBMI-related research in a number of labs.

*Chris Doe* used the microarrays developed by Johnson in a study describing the genetic program to create glia cells, which support nerve cell activity (Freeman, et al, 2003). The Doe and Johnson labs collaborated on a more complex microarray that allows them to identify the regulatory network controlling gene expression. The Doe lab uses this new microarray to uncover the logic circuit that produces one type of nerve cell versus another. The Johnson lab examined the way different genes are targeted by the same regulator in different tissues—the brain versus the respiratory system. The Johnson lab also completed a study using microarray to study of how different stress-regulated pathways regulate common and specific response genes.

b. The grant provided support for the fMRI facility and for the use of the fMRI facility by a number of BBMI affiliate faculty. Below are reports that provide detail on the kind of work done in this year.

Working together with the Lewis Center for Neuroimaging, *Postlethwait* and his associates (Smith, et al, 2004) succeeded in designing a coil that allows high resolution imaging of the brains of stickleback, zebrafish and other fish. One reason this is of great importance is the wide applicability of genetic findings with zebra-fish to other species including mammals discussed above. A second reason is that the Postlethwait group has been able to demonstrate the importance of single genes in evolutionary adaptation of a fish, the three spined stickleback. The stickleback has been an important fish for behavioral studies of aggression. Postlethwait's group studied the molecular biology that might underlie changes in the aggressive behaviors of fish.

The *van Donkelaar* lab initiated two projects examining the changes in brain activation patterns in patients who are recovering after brain damage. A project funded by the Centers for Disease Control, demonstrated that patients with a concussion have distinct attentional deficits as assessed behaviorally with the Attentional Network Test (ANT). This test separated components of attention related to attaining the alert state, orienting to sensory events and monitoring conflict between responses. The orienting and conflict components of attention appear to be affected by concussion, but not the alerting component. They examined whether these behavioral deficits have correlates in the pattern of brain activity in patients with concussion as assessed with fMRI. In addition, magnetic resonance spectroscopy was used to determine whether the neurochemistry

of the brain also altered in concussion and whether these alterations are confined to the areas underlying the behavioral deficits previously observed.

A second project, funded by the American Heart Association, examined how patients who have suffered a stroke recover function following an intensive form of physical therapy called constraint induced therapy. The fMRI was used to discover how this functional recovery is correlated with alterations in brain activation patterns. Furthermore, the extent of activation is being related to the degree of handedness prior to the stroke. The prediction is that the degree of handedness will determine the capacity for both functional recovery and brain activation alterations.

c. The grant provided additional support to build out the Transgenic Mouse facility and provided key support to a BBMI faculty member dependent on the facility. *Cliff Kentros* developed a model system in the mouse for examination of the relation of attention and memory (Kentros, et al, 2004). It was found that the activity of the location specific cells in the hippocampus depends upon engagement in a spatial task. It is assumed that attention to the spatial task is the critical factor in obtaining activation of the cells that code location. Kentros and colleagues (Agnihotri, et al, 2004) also reported that consolidation of memory by the hippocampus is dependent upon protein synthesis, since blocking such synthesis blocks long-term, but not short-term retention of new, but not old locations. Thus protein synthesis seems critical for consolidation, but not short-term memory or recall of already consolidated memories.

Kentros worked on the production of genetically modified mice designed for the dissection of the functional elements of neuronal circuits *in vivo*. The goal was the temporally regulated expression of a dominant negative transgene in a single neuronal cell type, enabling specific elements of neuronal circuits to be turned off during electrophysiological recordings of intact animals. This has been achieved by using a novel combination of existing transgenic technologies to “subtract” expression pattern of one promoter from another, maximizing anatomical specificity. He succeeded in generating the first genetically modified mice at the University of Oregon with support from this grant.

d. The grant provided partial support for the activities of BBMI affiliated cognitive neuroscientists and their relevant facilities.

*Michael Anderson* and colleagues (Anderson, et al, 2004) reported, in *Science* that people could be instructed to suppress the storage of new associations in memory. When they do so, they not only show reduced memory of the suppressed association, but they have reduced activation in the hippocampus, which is a crucial node of the network for storing memories and increased prefrontal activation in areas related to inhibitory control. These findings provide a strong experimental model for repression of memories. Johnson & Anderson (2004) have found that a similar inhibitory process may be important in normal forgetting of semantic facts.

In a review of the literature on the conditions for visual awareness *Mayr* (2004) argued that activation of the anterior cingulate, an important node of cognitive control, requires a conflict of which the person is consciously aware and is not triggered if the conflict remains outside of awareness. In a recent paper (Luu, et al., 2003) anterior cingulate activation has been shown to arise in the form of a theta rhythm in anticipation of feedback. Activity in this region was potentiated in depressed individuals in comparison with controls (Tucker, et al, 2003). Since individual differences in anterior cingulate activation have been related to several candidate

genes (Posner), it may be possible to predict which people are most likely to exhibit activation in this area under conditions of ambiguous exposure or enhanced feedback.

*Awh* and colleagues (Awh, et al, 2004) showed that the attentional blink, that serves to impair the report of a brief alphanumeric stimulus, does not impair face perception. This suggests that attention may be inhibited from processing two stimuli of the same category but not when they are of categories that have different visual system localizations. *Dassonville*, et al (2004) found that a visual illusion of location induced by a surrounding frame (Roelofs effect) is due to a perceived shift of the midline of the object toward the frame.

The *Neville* lab identified different neurocognitive systems that display different degrees of neuroplasticity throughout life (Capek, et al, 2004; Sanders, et al, in press; Roeder and Neville, 2003; Sanders and Neville, 2003). They conducted developmental studies of these different neurocognitive systems in children. The lab initiated a series of studies to assess the effects of different interventions on neural and cognitive development.

e. The grant provided major support for the activities of the Neuroinformatics Center (NIC) which completed installation of the ICONIC grid to provide high performance computing to BBMI relevant units. The ICONIC grid integrates three advanced IBM computing architectures on a shared area network multiple terabyte storage base, linked by microchannel fiber. This system is used by BBMI researchers to implement integration of information from hemodynamic, electrical and optical recording with much greater precision than was previously possible.

There were two primary software development projects implemented on the ICONIC (integrated cognitive neuroscience) Grid. The first project is statistical decomposition of dense array electroencephalographic (EEG) signals. The initial goal for this project was to extract noncephalic artifacts, including eyeblinks, eye movements, and cardiac potentials, from the EEG record. The second project was computational modeling of the electrical properties of the human head, including both electrical and optical transmission. The NIC had used independent component analysis (ICA) to remove artifacts due to eye blink and other noncephalic sources.

The NIC continued to develop a prototype system for telemedicine including applications to both military and civilian emergency medicine. Work focused primarily on applications to stroke. NIC is proposed to develop a 512 channel system that will combine electrical and optical imaging of the human brain (to be called HALO for head accessed laminar optoelectrics). The optical signaling uses a new technology that has been developed to achieve high signal sensitivity through the integration of avalanche photodiode detectors with laser diode optical sources.

## Dissemination of Information

Three workshops were successfully held during 2004.

January 15-16. Temporal coding in relation to imaging studies.

On Thursday evening Ron McKay provided an update on the creation of brain tissue via the use of stem cells. He described his efforts to develop active dopamine cells to a large and excited audience. On Friday afternoon Dr. McKay and Hillyard met with faculty graduate students and postdocs to review work in BBMI related to their expertise. A number of presentations were made and a lively discussion ensued. Friday afternoon Dr. Koretsky presented his work on

temporal coding using MRI method. Following his presentation, Dr. Hillyard presented combined fMRI-EEG methods for tracing the time course of neural activity.

April 16. The dedication of new mammalian genetics center.

An afternoon session allowed members of our group including Drs. Kentros, Marrocco, and Johnson to discuss with our guests work ongoing and anticipated in the mammalian genetics program. Our guest speakers, Dr Steve Soumi (primate behavior and genes) and Dr. Alcino Silva (mouse genetics) presented in the afternoon.

May 21-22. Brain, Learning and Curriculum.

Friday evening commenced with a presentation on dyslexia by Drs. Sally and Ben Shaywitz. A large audience of faculty, students and K-12 teachers and administrators were present. The next morning Dr. Dave Premack discussed the implications of his work on original intelligence for the design of a rational school curriculum. As a result of this highly successful workshop BBMI has set up a new Brain and Education committee to review and coordinate work between the College of Education and BBMI on the topic of brain and education.

## **Academic Year 04-05**

DoD's commitment of \$3million in FY04 helped to position the UO in its quest to address the most fundamental questions about the human brain and mind through combining its expertise in molecular biology, the genetics of neural development, and cognitive neuroscience. The support in FY04 supported the continuing development of the Neuroimaging and Neuroinformatics Centers, including technology transfer related to new instrumentation, measurement techniques, and software devoted to clinical applications, diagnostics, and modeling of brain processes. Particular emphasis was put on equipment upgrades to enhance the capacity of our cognitive neuroscience and mammalian genetics programs. A new research focus emerged bringing together faculty from cognitive neuroscience and education.

### Major Proposed Tasks

support for research projects at the NIC

salary support for technical assistance in the proteomics/genomics facility

support for scanning time on fMRI by BBMI affiliated faculty

support for personnel and technological developments at the fMRI facility

Support for cognitive neuroscience research projects including an emergent collaboration between cognitive neuroscience and College of Education faculty

Support for the Mouse Genetics Facility infrastructure development and support personnel

Lab renovation and equipment for cognitive neuroscience facility

### Accomplishments

#### Accomplishments of the Neuroinformatics Center

The NeuroInformatics Center (NIC) continued establishing high performance computing (HPC) resources with high-bandwidth networks and building web services and grid technologies for BBMI. In 04-05, the University of Oregon ICONIC (integrated cognitive neuroscience) Grid integrated seven multiprocessor clusters on a shared area network multiple terabyte storage base. All of the clusters run Linux and are connected by a high-speed gigabit network.

These HPC resources are used by BBMI affiliated faculty for distributed EEG and MRI measurement and analysis, neurological medical services, shared brain data repositories, remote and rural imaging capabilities. There were two major software development projects implemented on the ICONIC Grid at the NIC during this period.

The first project was statistical decomposition of dense array electroencephalographic (EEG) signals. The initial goal for this project was extraction of noncephalic artifacts, including eye blinks, eye movements, and cardiac potentials, from the EEG record. During the year Signal Cleaning Framework and performing research based upon APECS, Automated Protocol for Electromagnetic Component Separation was developed and tested.

In final testing, the NIC Signal Cleaning Framework implemented the Fast ICA and Infomax ICA algorithms on both distributed and shared memory parallel architectures using MPI and OpenMP, respectively. Written in C and incorporating ATLAS optimized BLAS Level2 and Level3, the Signal Cleaning Framework overcame the memory and performance limitations imposed on these algorithms by their MATLAB implementations. Preliminary testing of the Fast ICA implementation on both Intel Pentium Xeon and IBM Power4 based architectures revealed a 175-fold factor increase in performance over its MATLAB based counterpart. The Infomax implementation, based upon OpenMP, showed an increase in performance of ~ 400%.

The Signal Cleaning Framework can be invoked locally as a stand-alone program, from APECS (see below) or EEGLAB, developed by the Swartz Center for Computational Neuroscience at UCSD. This gives users of that program, if they have the proper hardware, simplified access to the Framework's memory and performance enhancements.

A job server that allows remote users to asynchronously dispatch job requests to and receive job results from the Signal Cleaning Framework over a distributed computing infrastructure was partially developed in this year.

APECS, an Automated Protocol for Electromagnetic Component Separation, identifies blink-related components derived from the ICA decomposition of input EEG data. Research performed with the assistance of APECS was presented at the Fifth International Conference in Independent Component Analysis and Blind Signal Separation (ICA-2004) in Granada, Spain and at the Cognitive Neuroscience Society's 2005 Annual Meeting in New York City (Glass, et al, 2004; Frank & Frishkoff, 2005a). A full-length paper was published in *Lecture Notes in Computer Science* (LNCS) 3195. Another full-length paper was prepared for submittal to *Journal of Computational Neuroscience* (Frank & Frishkoff, 2005b).

The second project was computational modeling of the physical properties of the human head, including both electrical and optical neuroimaging modalities. A multi-cluster computational environment with mixed-mode (MPI+OpenMP) parallelism for estimation of unknown regional electrical conductivities of the human head, based on realistic geometry from segmented MRI scans up to 256 x 256 x 256 voxels resolution, was developed. Accurate and robust 3D electrical and optical solvers for the forward problems were built on the base of the finite difference multi-component alternative directions algorithm (MCADI) and parallelized using OpenMP. The inverse problem was solved also in parallel across a distributed system of heterogeneous computational resources. The results were to be published at two major international conferences in the field (Salman, et al, working paper). At the meeting of the International Society for

Computational Science the paper on head conductivity received an award for excellence as one of the top papers presented.

The forward optical solvers developed on the base of MCADI have been used for solving PDEs describing other neuroimaging tomographic modalities, in particular, in simulation of photon migration (diffusion) in a human head in near-infrared spectroscopy of brain injuries and hematomas, fluorescence optical tomography of brain tumor, etc. (Turovets, working paper; Tucker, et al, ONR meeting paper; Tucker, Naleway & Turovets, meeting paper).

NIC continued to develop an application of a basic software package for a variety of inverse and imaging problems with real MRI data to estimate baseline realistic electrical/optical properties to be used in electrical source localization and electrical impedance tomography, hematoma/brain injury and tumor localization in the framework of DOT and fluorescence optical tomography problems.

#### Accomplishments of the proteomics/genomics facility

Much of the development of the brain and aspects of behavioral control are regulated by gene expression. The genomics facility, with TATRC funding in the form of salary support, has developed DNA microarrays for measuring gene expression on a global scale in eight model organisms in the past two years. These tools have furthered BBMI-related research in a number of labs, and introduced new possibilities to a number of others.

*Posner* worked with the genomics facility staff to examine the cellular and molecular basis for the neural networks that underlie self-regulation of cognition and affect. Alleles of several genes shown to be related to the function of this network were chosen for Restriction Fragment Length Polymorphism (RFLP) analysis. The facility isolated DNA from 18 individual cheek swab samples provided by the Posner group and used PCR to amplify the genes of interest. Restriction digests with appropriate enzymes were then performed to determine the genotype. Genotyping has been performed for six of the ten genes requested for analysis, including monoamine oxidase, dopamine transporter, neuronal nicotinic acetylcholine receptor, dopamine É-hydroxylase, dopamine D4 receptor A, and most recently brain derived neurotrophic factor. A paper showing the influence of DAT1 on shaping of attention networks during training is being developed.

The Genomics Facility pursued technologies to increase the scope of these and related studies, including using microarray technology and pyrosequencing for the purpose of analyzing a much larger number of genes influencing attention, increasing from 10 genes to thousands. Not only can we increase the number of genes analyzed by this method, but a larger number of individuals can be included in the study increasing the chance of finding significant differences.

*Chris Doe* used Drosophila microarrays in a study describing the genetic program to create glia cells, which support nerve cell activity (Freeman, et al, 2003). The *Johnson* lab created a novel Drosophila array called a genomic tiling path microarray that allows the genetic regulatory circuit underlying gene expression changes to be identified. The Doe lab used this new microarray to uncover the logic circuit that produces one type of nerve cell versus another. The Johnson lab examined the way different genes are targeted by the same regulator in different tissues°Xthe brain versus the respiratory system. The Johnson lab also completed a study using microarray to study of how different stress-regulated pathways regulate common and specific response genes.

c, d and e. Accomplishments of cognitive neuroscience faculty and the Lewis Center for Neuroimaging

How do we succeed in maintaining concentration on a target in the presence of distraction? *Awh, Sgarlata & Kliestik* (2005) showed evidence for a salience map related to locations at which irrelevant distracters might be presented. A further study used fMRI to show that activity in visual cortex prior to the presentation of a target acts to suppress a distracter when the target is presented (Serences, et al, 2005).

*Dassonville* carried out research raising questions about the need to postulate separate perceptual and motor effects in order to account for the illusion of the perceived location of a target depending upon the location of a surrounding frame (Roelofs effect). Prior research has shown conditions under which perception was prone to the illusions while motor actions were not and led to an idea of separate representation. The new research (Dassonville & Balla, 2005) showed that a single underlying representation could account for the dissociation.

Consolidation of a visually presented item over time and maintenance of that item within working memory are two of the processes involved in managing input. *Woodman & Vogel* (2005) showed that consolidation can take place just as well during maintenance of irrelevant items as when no such maintenance is required. This supports the two as independent processes operating within the same working memory space.

Great importance is attached to the time course of development of skills, particularly in the area of language. *Helen Neville* and her associates have used auditory evoked potentials to trace the brain organization of phonology (Mills, Prat, et al, 2004) and of semantics (Scherag, et al, 2004). They have also used the developmental method to explore the time course of the dorsal (motion) and ventral (color) pathways.

How do rules guide behavior? *Mayr* and *Bryck*, (2005) explored how hierarchical control guides successful priming of behavioral sequences. When the rule is preserved between successive trials priming is successful, but if the rule is not preserved the same type of priming is not successful. In a somewhat related study *Johnson-Frey* and his associates (Buxbaum, Johnson-Frey & Bartlett-Williams, 2005) explored the planning stage of motor production in patients with ideomotor apraxia. They found that deficits in motor imagery influenced performance in tasks with poor sensory feedback but not otherwise.

The *van Donkelaar* lab continued with two projects examining the changes in behavior, and brain activation patterns and biochemistry in patients who are recovering after brain damage. A project funded by the Centers for Disease Control has demonstrated that patients with mild traumatic brain injury (mTBI) have distinct attentional deficits as assessed behaviorally with the Attentional Network Test (ANT) (van Donkelaar, et al., 2005). In particular, the ability to orient attention and resolve visual conflict are deficient in this population, whereas the benefits associated with alerting stimuli are normal. Moreover, participants with mTBI require a proportionally longer time to respond during accurate task performance. These deficits appear to contribute to the problems this population has maintaining stability during gait while performing a secondary cognitive task (Parker, et al., 2005). By contrast, performance is normal on gap saccade task and RSVP tasks. This implies that the orienting deficit is not due to a problem disengaging attention and that attention can be distributed normally across time in the population, respectively. Using fMRI we have found that participants with mTBI activate a substantially larger swath of cortex than controls to perform the different components of the

ANT. In addition, brain metabolism as assessed with magnetic resonance spectroscopy (MRS) is abnormal for markers that probe neuronal integrity and cell membrane repair within 2 days of the injury, but returns to near baseline levels within 3 weeks.

A second project, funded by the American Heart Association, examined how patients who have suffered a stroke recover function following an intensive form of physical therapy called constraint induced therapy. Using fMRI they assessed how the therapeutic intervention influenced the pattern of activation in the motor areas of the brain during a simple hand gripping response. They began to analyze the change in the degree of asymmetry in the motor activation pattern as a result of the therapy relative to the degree of handedness pre-stroke.

Neville and her associates have begun to examine how different interventions may change performance in preschool children, particularly those who are eligible for Head Start because of low income. Preliminary work suggests that training in attention or music and training of parents can all have some impact on cognitive performance of these children. By use of scalp recordings the nature of the impact on attention is being examined.

Neville and Kamenui are working on research with young children first acquiring literacy. They plan to use a combination of large-scale educational studies with behavioral evaluations and neuroimaging to understand how various methods of teaching reading may shape underlying networks.

Posner & Rothbart (2005) have summarized evidence from neuroimaging and genetics that individual differences in cognitive networks can be related to genetic differences but that these networks can also be modified by specific educational experience related to self-regulation. Although everyone has this network the efficiency of its function is related to differences in genes. However, the network can be modified by specific educational experiences as well.

#### Accomplishments of Mouse Transgenic Facility and related faculty projects

In this year the Mouse Transgenic Facility was fully fitted out. As a result, faculty projects made substantial progress in 04-05.

Substantial progress was made in the Mammalian NeuroAnatomy Project (MNAP) in terms of subtractive genetics and developing transgenic lines of mice. Promoters require the use of large expanses of DNA inserted into bacterial hosts, called bacterial artificial chromosomes (BACs). A BAC containing a large portion of the kainate receptor subunit 1 (GRIK1) promoter is specifically expressed in CA3 pyramidal cells. The purpose of using this promoter region is simply to specify transgene expression in transgenic mice to CA3 pyramidal cells. Manipulation of BACs requires special shuttle vectors that enable RecA recombination in the bacterial host cells enabling insertion of a transgene into the BAC. The shuttle vector of choice is pLD53, originated by Drs. Gong and Heintz at Rockefeller University. Homology regions (rtTA2) were inserted at the start codon for the GRIK1 gene so that the GRIK1 promoter drives expression of rtTA2. PCR amplified the homology regions from the BAC and they were oriented properly around rtTA2 in a transition plasmid (pGEM) and then transferred the entire construct to pLD53. This completed shuttle vector was electroporated into the GRIK1 BAC host cells and co-integrates identified. They worked then on determining if resolution has occurred, which would signify insertion of the transgene into the BAC and removal of the rest of the shuttle vector. DNA was purified from resolved BAC hosts and injected into oocytes in the transgenic facility.

In addition, another major research direction of MNAP was to produce transgenic animals having conditional neuronal silencing. On the molecular level, this project was simply an extension of the MNAP project because the same conditional transactivator system was employed in both. For the animals used in neuronal silencing, a transgene that either prevents neuronal discharge or abolishes excitatory synaptic transmission was inserted downstream from the tetO promoter, which is sensitive to tTA and rtTA2. Thus, when a tTA or rtTA2 founder animal was crossed with a tetO/silencer founder animal, conditional neuronal silencing produced in a subset of the offspring. These animals were implanted with chronic extracellular unit recording headstages and tested in spatial learning and memory tasks.

A report on this subtractive strategy for the hippocampus was prepared for the November 2005 meeting of the Society for Neuroscience (Dumas, et al, in press). The studies reported the successful development of a mouse model in which subtraction of tTA label has been made in the hippocampus leaving only its cortical expression. This evidence provides proof of concept for the molecular anatomy subtractive method.

Work continued in the Marrocco lab to develop mice carrying out particular attention tasks. A version of both peripheral and central cue attention-shifting tasks was successfully developed for mice. Marrocco began to explore these tasks with DRD4 knockout mice in part to determine if they resembled previous findings with adult ADHD human subjects (Beane & Marrocco, 2004).

#### Cognitive Neuroscience facility support

Work began on the planning and renovation of the Posner and Keele Laboratories for Cognitive Science with support from the 04-05 TATRC grant. The facility, housed in Straub Hall with the department of Psychology and in close proximity to the Lewis Center for Neuroimaging, is the primary research space for BBMI researchers Ed Awh, Ulrich Mayr and Ed Vogel. It provides a shared EEG recording unit, eyetracker, MRI-guided transcranial magnetic stimulation unit and data analysis workstations. [http://psychweb.uoregon.edu/~pk\\_lab/facilities.htm](http://psychweb.uoregon.edu/~pk_lab/facilities.htm)

#### Academic Year 05-06

The UO used the continuing support of the DOD to support activities at the Lewis Center for Neuroimaging and the Neuroinformatics Center. The \$3 million in support allowed the UO to engage researchers on projects related to telemedicine, neuroinformatics, neuroimaging, cognitive neuroscience and genomics among other areas. The faculty hired in part through TATRC funds in years prior were all on campus during this period and began to establish full-fledged research activities. During this period BBMI faculty continued to explore opportunities for collaboration on specific projects with TATRC personnel in areas such as telemedicine and neuro-rehabilitation.

- partial support for NIC personnel and infrastructure development
- partial support for proteomics/genomics technician
- partial support for the operation of the fMRI center
- partial support for the operation of the Mammalian Genomics Facility
- support for brain and education research
- support for postdoctoral trainingships

#### Accomplishments

a. partial support for NIC Personnel and infrastructure development

The Neuroinformatics Center has continued to work on the GEMINI (Grid Environment and Methods for Integrated Neuro-Imaging) Project. The goal of the GEMINI project is to research and develop methods for delivering grid-enabled research tools to neuroinformatic researchers. We are currently developing optimized, multi-processor enabled EEG signal cleaners that integrate with popular tools. This work will transition into fully grid enabled services that can be easily accessed by researchers anywhere in the world. GEMINI is an ensemble of libraries, tools, and services that provides an robust and open environment for developing distributed applications in the neuroimaging domain. More complete information on the project and its architecture can be found at <http://www.nic.uoregon.edu/gemini/index.php>.

The [The Neuroinformatics Center](#) and the [GEMINI Project](#) have developed several high-performance tools to aid in the manipulation and interpretation of EEG data. We include implementations of the Infomax, FastICA and Sobi algorithms, as well as a framework to integrate these tools into Matlab and [EEGLAB](#). HiPerSAT version 1.1.alpha was released in March 2006 and is available free to the public for download via the NIC's website <http://www.nic.uoregon.edu/hipersat/index.php>. This version is under heavy testing right now as we shake the bugs out in anticipation of our next release. In this version we have support for both single and double precision computation, import of EGI Raw files, lots of bug fixes, and an improved interface. We will have a Windows binary download, as well as universal binaries for OS X. As always, the source is available if individuals want to build their own.

After conversations with Dr. Mogel and others at TATRC, we have shifted the NIC service delivery focus from rural telemedicine to MRI integration of the dense array EEG results with neurosurgical planning. Our site for this is Harborview Hospital, UW Seattle. The dense array EEG monitoring is in place, and we are now working out the pilot service delivery for the NIC/CDS networking capability. Target completion of the first phase is October 2006. An opinion piece in *The Lancet* (vol. 366, October 8, 2005) is an example of the interest in the epilepsy community over the advance in seizure localization made possible by NIC advances. The letter discusses how these advances may radically change current therapies if it is proven, through the kind of research at the NIC and EGI, that there is no such thing as a “generalized” seizure instead all should be treated as localized from the beginning.

## **Key Research Accomplishments**

Researchers at the NIC formulated a full-physics, full-geometry computational head modeling framework for simulating the electromagnetic properties of the human head. The framework development included the parallelization of simulation methods for high performance computation. The modeling tools are used for determining head tissue conductivity, EEG source localization and electrical impedance tomography.

NIC researchers created a framework for automating the evaluation of electromagnetic component separation methods with application to artifact removal from multi-channel EEG data. The framework included quantitative and qualitative criteria for evaluation, as well as the development of parallel signal analysis algorithms for EEG component decomposition.

NIC researchers designed a new approach and algorithms for automatic brain magnetic resonance image segmentation based on relative thresholding and morphological image analysis. The methods have been evaluated against leading state-of-the-art tools and shown to be more robust and accurate overall.

Discovery that "generalized" seizures of epilepsy are not initially generalized in the conventional sense, but arise from specific networks of the frontal pole and orbital frontal lobe by NIC affiliated researchers. These frontal networks appear to regulate thalamic projection systems which, in turn, regulate widespread cerebral regions, thereby explaining the generalized nature of the functional seizures. The advanced localization of dense-array EEG in this research was made possible by the improved head conductivity modeling recently developed at the UO NeuroInformatics Center.

The Kentros lab worked on the production of genetically modified mice designed for the dissection of the functional elements of neuronal circuits *in vivo*. The goal was the temporally regulated expression of a dominant negative transgene in a single neuronal cell type, enabling specific elements of neuronal circuits to be turned off during electrophysiological recordings of intact animals. This has been achieved by using a novel combination of existing transgenic technologies to "subtract" expression pattern of one promoter from another, maximizing anatomical specificity.

## **Reportable Outcomes**

Publications

See attached bibliography

Spin-offs

**Cerebral Data Systems (CDS)** is a company formed from an innovative collaboration of the UO's NeuroInformatic Center (NIC) and Electrical Geodesics, Inc., (EGI), a private company that designs, produces and sells electrophysiological neuroimaging equipment and related software. CDS is developing new techniques that allow more precise analysis of brain wave data by eliminating the distortion caused when brain signals pass through the skull to the scalp, where they are picked up by electrodes. These developments could provide a much more accurate map of where electrical activity is occurring in the brain, aiding researchers and physicians in evaluating and treating patients with epilepsy, stroke and other disorders and thereby improving their medical care. It also could be used in developing a better understanding of how the brain acquires and processes information.

Disclosures

There are two invention disclosures from the NIC in the 2005-2006 period, "Computation of skull conductivity with finite difference modeling" (Sergei Turovets, NIC) and "Cortical surface extraction with topology constraints" (Kai Li, NIC). This second one has been followed up by a patent application.

Patent

Name of Inventors: Cliff Kentros

Title of Invention: Subtractive Transgenics Serial #: 11/750,971 Election to file in US: Yes

Election to file foreign: No Confirmatory Assignment forwarded: Yes

Other related external funding

During this time period BBMI affiliated faculty were awarded some 300 individual grants totaling some \$50 million.

### **Conclusion**

The UO is looking forward to strengthening its relationship with TATRC through a new proposal for FY06 and FY07 that will focus on developing innovative and novel methods to improve neurorehabilitation for amputees and treatment for patients at remote sites with acute brain injury. The proposal builds on the infrastructure and discoveries supported in the Fy01-FY05 granting period.

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**Frey, S.H.**, & Danielmeier, C. (2006, October). "fMRI investigations on the role of the cerebellum in observational learning of manual skills." Paper to be presented at the Annual Meeting of the Society for Neuroscience. Atlanta.

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TATRC Related Faculty Awards  
 June 2001 through February 2006  
 Prepared by G. Chaffins

Start Date	PI Name	Sponsor	Project Title	Award \$	Grant #
Jun-00	Anderson, M	NIMH	Inhibitory Control and the Mechanisms of Forgetting	738,804	211210
Aug-05		U Cal Santa Cruz/NIH	The Impact of Emotion Regulation on Cognition in Aging	11,214	244890
Dec-04		Medical Research Foundation	Suppressing Unwanted Memories: Neural Systems of Intrusion Control	30,000	442840
Jun-02	Awh	NIH	Low-Level Constraints on High-Level Selection	582,198	211000
Jun-01		NIMH	Neural and Behavioral Mechanisms of Distractor Exclusion	690,298	211300
Dec-05		Medical Research Foundation	Diagnostic Tools for ADHD	29,977	446100
Jul-03	Barkan	NSF	Factor-Dependent Splicing of Chloroplast Group II Introns	430,524	205560
Jul-04		NSF	VCA - Plant RNA Binding Proteins: Tools for Functional Genomics and Application to Chloroplast Biogenesis	1,676,258	205910
Sep-01		NIH	IND-NRSA: Genetic Dissection of Intraorganellar Protein Sorting	79,044	213380
Aug-03		USDA	Biochemical Dissection of a Plant-Specific RNA Binding Domain	240,000	238310
Jun-01		US Israel Binational	crs1, A Nuclear Gene that Functions in the Splicing and Translation of Chloroplast mRNA's	3,000	390040
Oct-05		US Israel Binational	Nuclear Encoded RNA Splicing Factors in Plant Mitochondria	115,000	390050
Jul-03		American Heart Association	Biochemical Dissection of YhbY: An Assembly Factor for the Large Ribosomal Subunit in Bacteria	40,000	422080
Mar-03		Medical Research Foundation	YhbY: A Conserved Prokaryotic Protein Implicated in Ribosome Assembly	30,000	442320
Jun-04	Bradshaw	NSF	Dissertation Research: Circadian-Clock Genes and Variation in Photoperiodic Time Measurement: A Role for Timeless?	12,000	205880
Aug-04		NSF	Evolutionary Response to Rapid Climate Change	192,428	205970
Sep-04		NSF	Evolution of Photoperiodic Time Measurement in the Pitcher-Plant Mosquito, <i>Wyeomyia smithii</i>	46,124	206040
Aug-05		NSF	Evolution of Photoperiodic Time Measurement and the Circadian Clock in Animals: Perspectives from the Pitcher-Plant Mosquito, <i>Wyeomyia smithii</i>	123,301	206180
Dec-02	Dassonville	Medical Research Foundation	Reference Frames for Visual Perception and Action	29,936	442260
May-04	Doe	NIH	INST-NRSA: Developmental Biology Training Program	576,068	216340
Jul-01		American Cancer Society	Postdoctoral Fellowship: Genetic, Molecular, and Computational Analysis of Glial Development	118,000	421780
Jan-03		American Heart Association	Requirement of Lis1 and Glued for Spindle Orientation in <i>Drosophila</i> Epithelial Cells and Neural Precursor Cells	41,250	422010
Jan-06		American Heart Association	Identification and Function of Proteins Required for Neuronal Polarity	145,284	422490
Apr-03		Damon Runyon Cancer Fund	Approaching Neuronal Polarity in <i>Drosophila</i>	128,500	442300
Aug-03		Damon Runyon Cancer Fund	Regulation of Neural Stem Cell Self-Renewal	128,500	443280

Sep-04	Frey	NIMH	Ventral and Dorsal Visual Streams in Action Planning	248,794	211790
Sep-04		Emery U/McDonnell	Ventral and Dorsal Visual Streams in Action Planning	63,385	442750
Oct-04		Dartmouth U/McDonnell	Beyond Localization: Reconsidering the Issue of Category-Specific Visual Areas	9,136	443320

Jan-03	Johnson (E)	American Heart Association	Genetic and Genomic Dissection of Hypoxia Regulatory Pathways in Drosophila	80,000	422000
Jun-03		American Cancer Society	Identity and Function of Hypoxia-Response Genes	720,000	422030
Jul-03		American Heart Association	Identification of Hypoxia-Response Genes in Drosophila melanogaster	91,340	422190
Jun-02		Medical Research Foundation	Identification of Hypoxia-Response Genes in Drosophila	30,000	442070

Dec-04	Kentros	Medical Research Foundation	Pharmacological Modulation of a Hippocampal Representation	29,954	442850
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Sep-03	Malony	NSF	Acquisition of the Oregon ICONIC Grid for Integrated COgnitive Neuroscience Informatics and Computation	1,037,521	205660
Nov-04		NSF	ST-HEC: Collaborative Research: Scalable, Interoperable Tools to Support Autonomic Optimization of High-End Applications	230,134	206060
Aug-01		Dept. of Energy	Performance Technology for Tera-Class Parallel Computers: Evolution of the TAU Performance System	999,318	230530
Aug-03		Dept. of Energy	Performance Engineering Technology for Scientific Component Software	1,151,724	234050
Dec-04		Argonne/Dept. of Energy	Extreme Performance Scalable Operating Systems	194,806	234100
Apr-05		Dept. of Energy	Application-Specific Performance Technology for Productive Parallel Computing	250,527	234220
Oct-02		Army MRAA	Oregon Neuroinformatics Center (NIC)	2,060,370	235810
Aug-03		Computing Research Assoc./NSF	Computational Environment Infrastructure with Applications to Mid Ocean Ridge Research: The 'Virtual Research Vessel' Prototype	26,562	244790
Feb-02		Lawerence Livermoore/DOE	A Database Framework for Large-Scale Parallel Performance Analysis	150,000	270430
May-03		Lawerence Livermoore/DOE	Tri-Labs ASCI Level 3	450,000	270540
Dec-02		Univ. Utah/LLNL	Performance Tools for the Unitah Computational Framework and C-SAFE Applications	284,000	270590

Sep-01	Marrocco	NIH	The Neurochemistry of Visuospatial Attention	701,506	210960
Dec-05		Medical Research Foundation	Cholinergic Mechanisms of Reflexive Attention	29,994	446110

Sep-02	Mayr	American Psychological Association	Developing Individuality in the Human Brain: A Festschrift in Honor of Michael Posner	10,004	442340
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Apr-02	Neville	NIH	Development of Cerebral Specializations	1,897,369	210980
Sep-03		NIH	Neurobehavioral Development: Normal, LI and Deaf Children	1,606,548	211480
Jan-04		NIH	IND-NRSA: Auditory Processing of Biological and Linguistic Stimuli	47,296	213480
Apr-04		Army MRAA		1,161,256	235840
Nov-02		Intern. Human Frontiers Science P	Plasticity and Specificity in the Developing Brain	260,323	442230
Jul-04		Dartmouth Col/Dana Foundation	Arts Education and Its Impact on the Brain and Enhanced Learning in Other Knowledge Domains	66,667	442870

Jan-03	Nunnally	Siemens	Siemens Master Research Agreement for fMRI Collaboration	270,000	413680
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Jul-04	Posner	Dartmouth Col/Dana Foundation	Arts Education and Its Impact on the Brain and Enhanced Learning in Other Knowledge Domains	66,667	442880
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Mar-03	Postlethwait	NSF	Genetic Basis of Morphological Evolution in Stickleback	519,948	205340
Jul-04		NSF	Non-vertebrate Chordate Oikopleura and Evolution of Vertebrate Development Innovations	280,000	205920
Jun-05		NSF	IGERT Formal Proposal -- Integrated Training in the Evolution of Development	1,194,994	206250
Apr-03		NIH	Genomic Analysis in Zebrafish Development	1,273,370	211810
Apr-05		NIH	Resources for Teleost Gene Duplicates and Human Disease	534,641	212180
Feb-01		NIH	IND-NRSA: Quantitative Trait Loci Mapping in Threespine Stickleback	118,000	213350
Aug-04		Oregon State U/NIH	Mutant Lines of Zebrafish Highly Sensitive to Neoplasia (subcontract)	57,600	245030
May-02		Spanish Ministry of Education	Postdoctoral Fellowship for Cristian Canestro	36,000	385070
Sep-04		Franconi Anemia Foundation	A Zebrafish Model for Fanconi Anemia	88,242	442830

Sep-01	Remington	NSF	Structure-Function in Red and Yellow Fluorescent Proteins	375,000	204810
Aug-04		NSF	Photodynamics and Maturation of Coral Fluorescent Proteins	350,000	206030
Jan-05		NIH	Development of Fluorescent Protein Biosensors	254,945	212100
Sep-05		US Israel Binational	Time-Resolved Study of Excited State Proton Transfer in the Green Fluorescent Protein and its Mutants	6,000	380100
Jan-06		American Heart Assoc	Development of a Green Fluorescent Protein Based Redox Sensor for Use in Oxidizing Cellular Environments	48,000	422480

Feb-02	Selker	NSF	Genetic Analysis of Silenced Chromatin in Neurospora	575,000	204920
Sep-02		NIH	Genetic Aspects of DNA Methylation	1,894,335	211390
May-02		Georgia Tech/NIH	Fused Pyrimidine (IsoA) Nucleosides: Design, Synthesis and Biological Investigations	12,903	242940
May-03		U Maryland Baltimore/NIH	Fused Pyrimidine (IsoA) Nucleosides: Design, Synthesis and Biological Investigations	122,097	243780
Jun-01		American Heart Assoc	AHA Summer Science Student Fellowship	3,000	421760
Jul-02		American Heart Assoc	Characterization of SET Proteins from Neurospora crassa and their Possible Roles in Histone Modification and DNA Methylation	72,615	421870
Jan-04		American Cancer Society	Mechanisms of Telomeric Gene Silencing in Neurospora crassa	125,000	422120
Oct-04		American Cancer Society	The Control of DNA Methylation	124,878	422290

Jun-04	Sereno	Medical Research Foundation	Functional MRI of 3-D Shape in Human Cortex	30,000	442680
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Jul-02	Tucker	NIMH	IND-NRSA: Electrophysiological Effects of Emotion in Semantic Processing	28,257	211350
Jul-02		NIMH	IND-NRSA: Electrophysiological Effects of Emotion in Semantic Processing	58,326	213410

Feb-03	Weeks (J)	NIH	IND-NRSA: Mechanisms of Steroid-Mediated Synaptic Plasticity	93,140	213430
Mar-03		NIH	IND-NRSA: Genomic and Proteomic Analysis of Heroin Administration	98,696	213470
Jun-04		OHSU/Alzheimer Association	A Drosophila Model of Neuroprotection by Steroid Hormones	21,100	300230
Jul-04		Muscular Dystrophy Assoc	A Novel Screen for Muscle and Motoneuron Death and Protection Genes	145,669	422300
Jan-03		National Alliance for Schizophrenia	Genomic and Proteomic Analysis of Post Mortem Schizophrenia Tissue	54,889	442380
Sep-03		Medical Research Foundation	Steroid-Mediated Neuroprotection: A Novel Cell Culture System in Drosophila	30,000	442480

Sep-01	van Donkelaar	NSF	Brain Mechanisms Underlying Sensorimotor Adaption	45,028	204790
Jul-04		American Heart Association	Handedness and Cortical Plasticity in Stroke Rehabilitation	198,000	422250
Sep-03		Medical Research Foundation	Cortical Correlates of Functional Recovery Following Stroke Rehabilitation	30,000	442490

Dec-03	Vogel	NIMH	Updating Representations in Visual Working Memory	140,677	211450
Sep-04		Medical Research Foundation	Neural Measurements of Working Memory Capacity	29,982	442730